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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/946,138	10/07/97	ALBRECHT G	808-2

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EXAMINER	
TUNG, J	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/946,138	Applicant(s) Albrecht et al.
	Examiner Joyce Tung	Group Art Unit 1807

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-29* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-29* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Double Patenting

1. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." . Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

2. Claims 1-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-29 of copending Application No. 08/862,610. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented

3. The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

4. Claims 1, 2, 6-8 and 11-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, 10, 18, 20, 34, 40, 42, 44, 48-50 and 53 of U.S. patent NO: 5,599,675. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, 6-8 and 11-12 in the instant application disclose an encoded adaptors having nuclease recognition site used to ligate to a polynucleotide for determining the nucleotide sequence of the polynucleotide. The encoded adaptors have the same structure as the probe in U.S. patent NO: 5,599,675. Further the encoded adaptors have an oligonucleotide tag which hybridizes to a tag complement which can generate a fluorescent signal. This is obvious in view of claim 49 in the patent which discloses the probe comprising a first single stranded oligonucleotide and a second single stranded oligonucleotide. The end of the first oligonucleotide is complementary to the protruding end of the polynucleotide and the second oligonucleotide is complementary to the first oligonucleotide to form a duplex containing a nuclease recognition site. The probe is also labeled with fluorescent dye.

5. Claims 15-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 11-12, 21, 25 and 27 of U.S patent NO: 5,604,097 in view of U.S. patent NO: 5,599,675. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 15-18 in the instant application disclose a method for determining a nucleotide sequence of a polynucleotide comprising the steps of attaching, sampling, sorting, ligating and identifying. These steps are obvious over claims 1-3, 11-12, 21, 25 and 27 of U.S patent NO: 5,604,097 which disclose a

method for determining a nucleotide sequence of a polynucleotide including the steps of attaching, sorting and identifying and in view of U.S. patent NO: 5,599,675 which discloses a method for determining a nucleotide sequence including the step of ligating.

Claim Rejections - 35 USC § 112

6. Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. These claims are confusing because of the language "encoded adaptors" and "a minimally cross-hybridizing set". It cannot be determined what is encompassed.

b. Claims 1-23 are confusing because it is not clear how the "ligating" step takes place without ligase.

c. Claims 15-18 are confusing because it is not clear how the "attaching" step takes place.

e. Claims 1-16 and 19-22 are confusing because of the language "the nucleotide sequence" in claims 1 and 19 or "the nucleotide sequences" in claim 15 which has no antecedent basis.

f. Claims 24-29 are confusing because of the language "said single stranded moiety $(N)_t$" in claims ~~25~~ 24 and "said double stranded moiety" in claim 28. These languages have no antecedent basis.

g. Claims 15 and 16 are confusing because of the language "the one of more encoded adaptors" in claim 15 which has no antecedent basis.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-10, 12-14 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (5,599,675).

Claim 1 is draw to a method to determine the nucleotide sequence at an end of a polynucleotide. The method comprises: ligating encoded adaptors to an end of the polynucleotide in which the adaptors have an oligonucleotide tag selected from cross-hybridizing oligonucleotide and a protruding strand complementary to a portion of the polynucleotide and identifying the nucleotide in the polynucleotide by hybridizing the oligonucleotide tag to a tag complement.

Claims 2-7 recite further limitations to claim 1 in which a plurality of different encoded adaptors ligates to the end of the polynucleotides via hybridization between the protruding strand of the adaptor and the portion of the strand of the polynucleotide, and the portions of the strand of the polynucleotide are contiguous. The protruding strand of the adaptor has 2-6 nucleotides. The identification step includes hybridizing the fluorescent labeled tag complement to the oligonucleotide tag and the identity of each nucleotide in the polynucleotide is determined.

Claims 8-10 and 12-14 recite further limitations to claim 1 in which the structure of the encoded adaptor is described.

Claims 19-23 are drawn to the same method as described above in claims 1-10 and 12-14.

Brenner '675 discloses a method of nucleic acid sequence analysis in which a probe used to ligate to the terminus of a target polynucleotide and a nucleotide is identified in the protruding strand of the target polynucleotide. The probe has a complementary protruding strand to the protruding strand of the target, nuclease recognition site (see column 6, lines 20-30) and is labeled by fluorescent moiety. In another embodiment the probe is ligated to one end of the target forming a ligated complex and a second single stranded oligonucleotide is complementary to the protruding strand of the ligated complex (see column 9, lines 35-54) which can be cleaved by nuclease (see column 15, lines 41-45). The protruding strand of the probe is consisted of four nucleotides (see column 10, lines 24) and the duplex formation region of the probe is about 15-25 base pairs (see column 11, lines 1-4). The method can also applied to a plurality of different portions of a target polynucleotide (see column 16, lines 15-19).

Brenner '675 does not disclose an encoded adaptor which ligates to an end of a target polynucleotide for determining nucleotide of a nucleic acid sequence, while the method of Brenner '675 uses a probe to ligate to an end of a target polynucleotide. However, the structure of the probe are the similar with the encoded adaptor. Additionally, the method steps are similar with the steps in claims 1-7.

One having ordinary skill in the art would have been motivated to use an encoded adaptor in the method of Brenner to determine a nucleic acid sequence because it would have been

expected to serve the same purpose as the probe of Brenner. It would have been prima facie obvious to carry out the method as claimed.

9. Claims 11 and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (5,599,675) in view of Brenner (5,604,097).

Claim 11 recites further limitations to claim 1 in which the oligonucleotide tag of the encoded adaptor is double stranded and the tag complements are single stranded. The specific hybridization forms a Hoogsteen triplex

Claims 15-16 are drawn to a method to determine the nucleotide sequence of a plurality of polynucleotides. The ligation and identification of nucleotide are the same as the step described in claim 1. Additionally the method includes attaching a first oligonucleotide tag to the polynucleotide, sampling the polynucleotide based on the different oligonucleotide tag attached and sorting the polynucleotide by hybridizing the first oligonucleotide tag to its respective complements attached on a solid support.

Claim 1 is rejected under 103 over Brenner (5,599,675) in paragraph8.

The teachings of Brenner ('675) are stated in paragraph 8.

The '675 patent does not disclose a method which includes the formation of the Hoogsteen triplex and the steps of attaching a first oligonucleotide tag to the polynucleotide, sampling the polynucleotide based on the different oligonucleotide tag attached and sorting the polynucleotide by hybridizing the first oligonucleotide tag to its respective complements attached on a solid support.

The '097 patent discloses a method of tracking, identifying and sorting polynucleotide by using oligonucleotide tags (see column 35, lines 1-18), and the formation of the Hoogsteen triplex for identifying nucleic acid sequence (see column 5, lines 51-56).

One having ordinary skill in the art would have been motivated to combine both the teachings of patents of Brenner because the patent '097 teaches the steps of attaching, sampling and sorting the polynucleotide and the patent '675 teaches the steps of ligating, cleaving and identifying. The combination of the teachings of both patents would have determined a nucleic acid sequence of a polynucleotide. It would have been prima facie obvious to carry out the method as claimed.

10. Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (5,604,097) in view of Brenner (5,599,675).

Claims 17-18 are drawn to a method to identify a population of mRNA molecules. The steps involve forming a population of cDNA from the population of mRNA molecule, then the steps of sampling and sorting the cDNA molecules are the same as the steps in claims 15-16, and the ligating and determining the identity of the cDNA are the same as the steps in claim 1.

Brenner '097 discloses a method to identify a population of mRNA molecules including the steps of forming a population of cDNA, sorting the cDNA, determing the nucleotide sequence of the cDNA and identifying the population of mRNA (see column 36, lines 28-53).

Brenner '097 does not disclose that the method includes the steps of ligating and cleaving.

Brenner '675 discloses a method for identifying nucleotide sequence which includes ligating and cleaving steps for identifying nucleotide sequence. The details are in paragraph 8 above.

One having ordinary skill in the art would have been motivated to combine the teachings of both patents of Brenner because the patent of '097 teaches forming a population of cDNA from mRNA, sorting the cDNA, determining the nucleotide sequence of the cDNA and identifying the population of mRNA, and the patent of '675 teaches ligating and cleaving steps for identifying the nucleic acid sequence of DNA. Therefor, it would have been prima facie obvious to carry out the method as claimed.

11. Claims 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (5,604,097).

Claims 24-26 are drawn to a composition in which a double stranded oligonucleotide adaptor has a single stranded moiety which is a member of a minimally cross-hybridizing set.

Claims 27-29 are drawn to a composition in which a double stranded oligonucleotide adaptor has a double stranded moiety which is a member of a minimally cross-hybridizing set.

Brenner '097 discloses oligonucleotide tags which are double stranded for identifying or sorting nucleic acid and containing a subunit 3-6 nucleotides in length selected from a minimally cross-hybridizing set (see Abstract). The subunit can form a duplex or triplex.

One having ordinary skill in the art would have been motivated to construct a composition comprising the oligonucleotide tags to identify nucleic acid sequence because Brenner '097

indicates that the use of oligonucleotide tags is for identifying or sorting nucleic acid sequence and the oligonucleotide tags has the same structure as taught by Brenner '097 in which the oligonucleotide tags is single stranded and complementary to its respective complement comprising a single strand. It would have been prima facie obvious to construct the oligonucleotide adaptors composition as claimed.

12. No claims are allowable over the prior art.

13. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal

Mall 1 using (703) 305-3014 or 305-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

February 9, 1998

W. GARY JONES
SUPERVISORY PATENT EXAMINER
AU 1634
2/13/98